REMARKS

Claims 21-31 are currently pending in the application. Amendments to the claims are fully supported by the specification and do not introduce new matter and/or raise new issues requiring further consideration and/or search. Entry of the amendments is requested.

Rejection under 35 U.S.C. 102

Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated by WO97/23614 (Boyle et al.). The Examiner argues that Claim 21 encompasses OPG having amino acids 22-401 of SEQ ID NO:2 and is therefore anticipated by WO97/23614, which teaches "a fusion protein comprising an OPG variant 22-401 fused at the N-terminus to the C-terminus of the Fc protein ... "

Without acquiescing to the rejection and solely to advance prosecution, Applicants have amended Claim 21 to recite an OPG variant or fragment which has a deletion of one or more amino acids from positions 186-401 as shown in Figure 2 (SEQ ID NO:2) or has an amino acid sequence from positions 22-X as shown in Figure 2 (SEQ ID NO:2) wherein X is any residue from position 185 to 293 inclusive. It is believed that the rejection may be withdrawn.

Rejection under 35 U.S.C. 103

Claims 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO97/23614 (Boyle et al., hereafter "Boyle") as applied to Claim 21 and further in view of WO98/28427 (Mann et al. hereafter "Mann") Both articles were cited by Applicants. The Examiner argues that one skilled in the art would have been motivated to make the claimed OPG fusion proteins and would have had a reasonable expectation of success in doing so. Applicants disagree.

The results obtained with the claimed Fc-OPG fusion proteins are unexpected as one skilled in the art could not have anticipated that addition of an Fc region to the amino terminus of an OPG polypeptide fragment would enhance OPG activity of increasing bone density. By way of example, Table 3 demonstrates that the Fc-OPG fusion polypeptide met-FcdC-OPG[22-194] has greater *in vivo* activity than that of met OPG[22-194], the corresponding unfused OPG polypeptide fragment, which is shown in Table 2. There was no suggestion that such a result could have been obtained by constructing an Fc fusion to the amino terminal end of an OPG polypeptide fragment.

The Examiner argues that Boyle teaches modifications at the N-terminus or C-terminus of OPG which would lead one to conclude that fusion of an Fc molecule at either the N-terminus or the C-terminus of OPG would give an active molecule. Although the Examiner does not refer to any specific modifications, Applicants note

that Boyle disclosed truncations of amino acids at the N-terminal and C-terminal ends of OPG, which have OPG activity. However, one skilled in the art would appreciate that fusion of an Fc region to OPG can lead to an OPG polypeptide may be structurally and/or functionally different from one that is only truncated. Accordingly, an OPG fusion protein would not be considered an obvious variant of a truncated OPG polypeptide.

The Examiner also argues that Boyle teaches the conjugation of a polyethylene glycol (hereafter "PEG") molecule to the N-terminus of OPG. In view of this disclosure, the Examiner alleges that one skilled in the art would reasonably conclude that molecules other than PEG can be conjugated to the N-terminus of OPG and still retain activity. For the reasons set forth above, there is no basis for one skilled in the art to conclude that addition of a PEG molecule to the N-terminus of OPG would render obvious the fusion of an Fc polypeptide to the N-terminus of an OPG polypeptide fragment. The resulting molecules are likely to be structurally and functionally different from each other and there is no assurance that an Fc molecule fused to an OPG polypeptide fragment would be similar to a PEG modified OPG polypeptide fragment.

In view of these remarks, the rejection should be withdrawn.

CONCLUSION

Claims 21-31 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

Robert B. Winter
Attorney/Agent for Applicant(s)
Registration No.: 34,458
Phone: (805) 447-2425
Date: October 23, 2003

Please send all future correspondence to:

US Patent Operations/ RBW
Dept. 4300, M/S 27-4-A
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, California 91320-1799